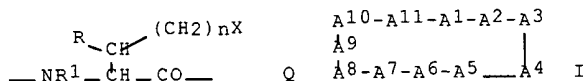


L35 ANSWER 222 OF 272 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1989:232108 HCAPLUS Full-text  
DOCUMENT NUMBER: 110:232108  
TITLE: Cyclosporins and pharmaceutical compositions  
containing them  
INVENTOR(S): Galpin, Ian James  
PATENT ASSIGNEE(S): National Research Development Corp., UK  
SOURCE: Eur. Pat. Appl., 28 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 300785	A2	19890125	EP 1988-306697	19880721
EP 300785	A3	19900523		
EP 300785	B1	19931201		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
GB 2208294	A1	19890322	GB 1988-17434	19880721
GB 2208294	B2	19910424		
US 5079341	A	19920107	US 1988-222211	19880721
AT 97916	E	19931215	AT 1988-306697	19880721
JP 01151600	A2	19890614	JP 1988-184461	19880722
PRIORITY APPLN. INFO.:			GB 1987-17300	A 19870722
			EP 1988-306697	A 19880721
OTHER SOURCE(S):	CASREACT 110:232108; MARPAT 110:232108			
GI				



AB Cyclosporins in which the amino acid residue at position 1 is either derived from 2-carboxyazetidine, 2-carboxypyrrolidine, or 2-carboxypiperidine, which may optionally be substituted on a ring C atom other than that at position 2 by an amino, methylamino, mercapto, or hydroxy group, said group optionally being in derivative form, and/or by an acyclic aliphatic hydrocarbon group, or is an amino acid residue Q (n = 0, 1, 2; R = H, acyclic aliphatic hydrocarbyl; R1 = H, Me; X = NH2, MeNH, SH, OH) are prepared. The said cyclosporins may have formula I [A1 = residue of 2-carboxyazetidine, 2-carboxypyrrolidine, or 2-carboxypiperidine, which may be substituted by Q, etc.; A2 = imino; A3 = sarcosine residue; A4 = N-methylleucine residue; A5 = Val; A6 = N-methylleucine residue; A7 = A8 = Ala; A9 = N-methylleucine residue; A10 = N-methylleucine residue or sarcosine residue; A11 = N-methylvaline residue; or such a cyclic undecapeptide in which one or more of any amino, methylamino, mercapto, or OH group present in A1 or A2 is in derivative form]. The above cyclosporins are useful as antiinflammatories, immunosuppressants, and antibacterials. H-(Me)Thr-Abu-Sar-(Me)Leu-Val-(Me)Leu-Ala-D-Ala-(Me)Leu-(Me)-Leu-(Me)Val-OH [Abu = 2-aminobutyric acid residue; Sar = sarcosine residue] in CH2Cl2 was treated with DMAP and the Castro reagent BOP to give cyclo[(Me)Thr-Abu-Sar-(Me)Leu-Val-(Me)Leu-Ala-D-Ala-(Me)Leu-(Me)Leu-(Me)Val] (II). The immunosuppressant activity of I was compared with that of cyclosporin A (CsA) in mixed leukocyte culture using mouse lymphocytes and allogeneic dendritic cells (DC). The uptake of 3H thymidine for incorporation into DNA was >50% higher for II at 8 µM than for CsA at 8 µM.

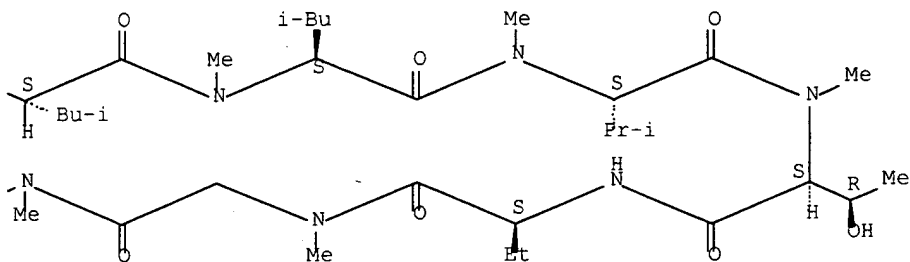
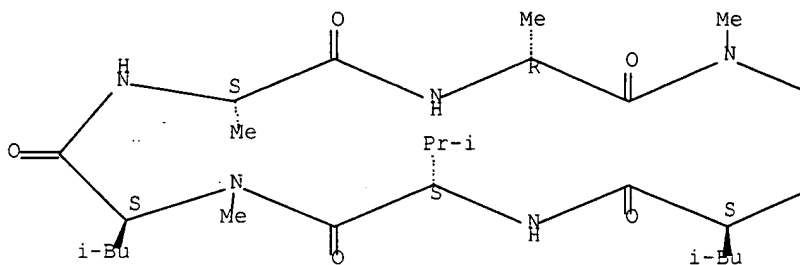
IT 101772-27-4P 116236-54-5P 116236-55-6P  
116236-56-7P 116236-57-8P 116236-59-0P  
116266-02-5P 116847-16-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation of, as antibacterial, antiinflammatory, and immunosuppressant)

RN 101772-27-4 HCAPLUS

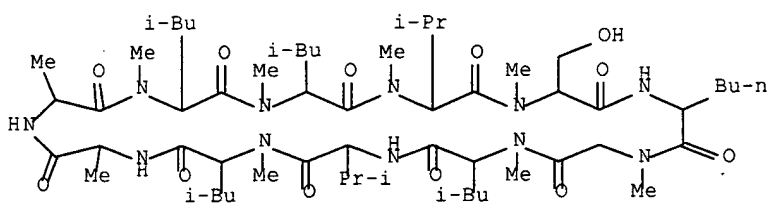
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Absolute stereochemistry.



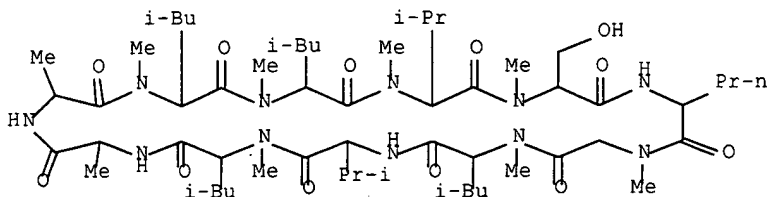
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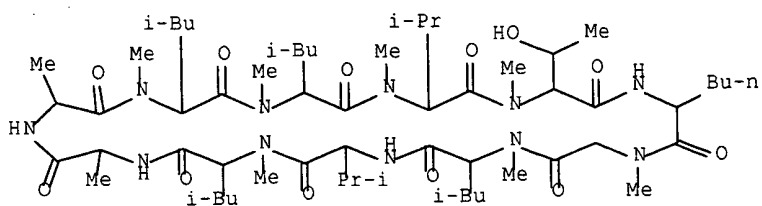
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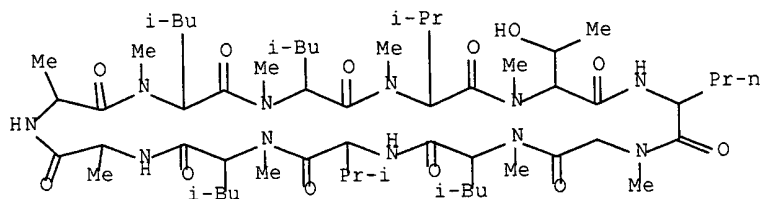


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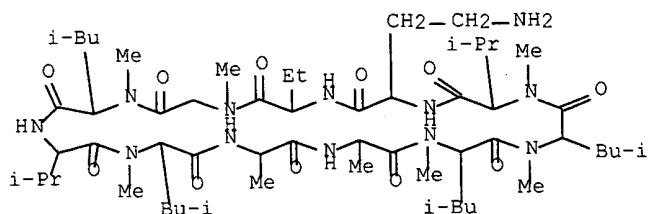
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RN 116236-57-8 HCAPLUS  
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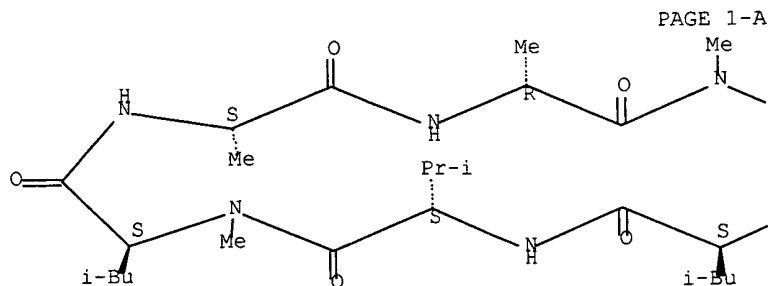


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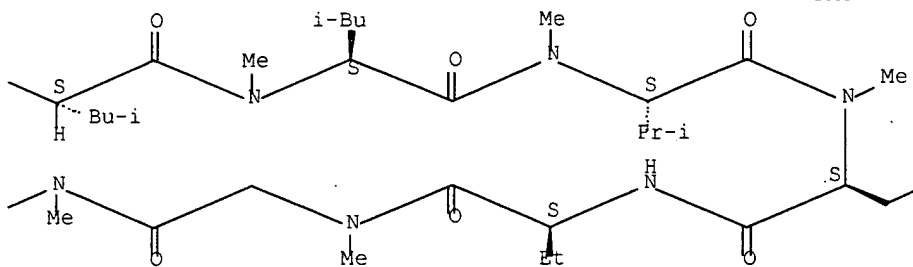
RN 116266-02-5 HCAPLUS  
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Absolute stereochemistry.



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PAGE 1-B

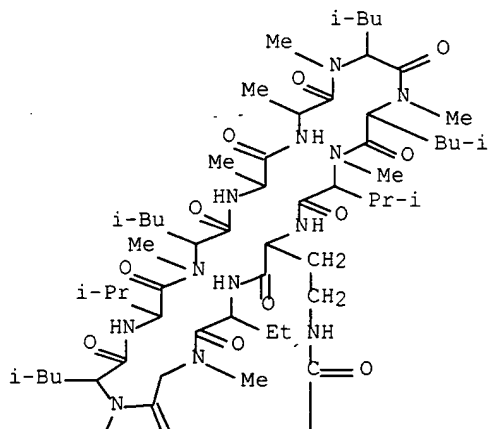


PAGE 1-C

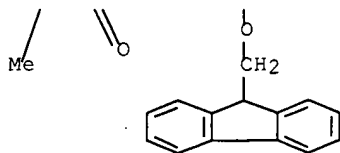
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RN 116847-16-6 HCAPLUS  
 CN Cyclosporin A, 6-[N4-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-2,4-diaminobutanoic acid]- (9CI) (CA INDEX NAME)

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PAGE 2-A



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